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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/528,377

01/04/2006

Jeffrey S. Glenn

STAN-316

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07/11/2008

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EXAMINER

LUCAS, ZACHARIAH

ART UNIT

PAPER NUMBER

1648

MAIL DATE

DELIVERY MODE

07/11/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

1. Claims 1, 3, 5-23 are pending in the application.
2. In the prior action, mailed on August 23, 2007, claims 1-21 were pending; with claims 1-10 under consideration and rejected; and claims 11-21 withdrawn from consideration.
3. In the Response of June 11, 2008, the Applicant amended claims 1, 5, 8-10; cancelled claims 2 and 4; and added new claims 22 and 23.
4. Claims 1, 3, 5-10, 22, and 23 are under consideration.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on February 19, 2008 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Drawings

6. **(Prior Objection- Withdrawn)** The drawings are objected to because the description of Figure 8 indicates that there should be two sets of bars, one white and the other hatched; however all of the bars presented in the Figure were white. In view of the amendment of the Figure, the objection is withdrawn.

Claim Objections

7. **(New Objection)** New claim 23 is objected to because of the following informalities: the term "aid" in line 1 of the claim should read "said." Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. **(Prior Rejection- Withdrawn)** Claims 1-10 were rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In view of the amendment of the claim, the rejection is withdrawn.

9. **(Prior Rejection- Withdrawn)** Claim 4 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of the claim, the rejection is withdrawn.

10. **(Prior Rejection- Withdrawn)** Claim 5 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendment of the claim, the rejection is withdrawn.

11. **(Prior Rejection- Withdrawn)** Claims 1 and 3-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims were rejected on two grounds. First, each of the claims is rejected for exceeding the scope for which adequate descriptive support has been provided because the application demonstrates possession of only one species of the claim genus (showing only that the HCV NS4B protein binds RNA or GTP, and has GTPase activity). Secondly, claim 5 is also rejected because the application does not provide descriptive support for methods of screening for “an RNA binding activity,” as the application has disclosed only the ability of the protein to bind RNA, and not what activities the

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protein is performing that involves such RNA binding. In view of the amendments to the claims, both grounds of rejection are withdrawn.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. **(Prior Rejection- Maintained)** Claims 1-4 were rejected under 35 U.S.C. 103(a) as being unpatentable over Del Vecchio et al. (WO 99/01582- of record in the April 2006 IDS) in view of the teachings of Jin et al. (Arch Biochem Biophys 20:47-53), Kadaré et al. (J Virol 70:8169-74), and Rodriguez et al. (JBC 268:8105-10). The claims have been amended to require that the NS4B polypeptide is an HCV NS4B polypeptide. The amendment does not affect the rejection. The rejection is withdrawn from cancelled claims 2 and 4.

The Applicant traverses the rejection on the remaining claims based on the assertion that in order to reject claims by combining prior art elements according to allegedly known methods to yield predictable results, the Office must articulate three enumerated findings described on pages 7 and 8 of the Response. This argument is not found persuasive. The three part test provided by the Applicant is only one of a multiplicity of potential tests for finding obviousness.

An alternative test provided by the Federal Register submission cited by the Applicant is the “Obvious to Try” test (provided on page 57532 (left column) of the indicated Federal Register submission). This test also sets forth three findings that must be shown. First, the Office

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must show that there was a recognized problem of need in the art. In this case, the art teaches that there was a need in the art for inhibitors of the HCV NS4B protein as potential inhibitors of HCV infection.

Second, the test requires a finding that there were a finite number of potential predictable solutions to the problem. The teachings in the primary reference indicate that the NS4B protein binds to ATP and acts as an ATPase. However, the teachings in the secondary reference indicate that other ATPases known in the art also act as GTPases, and that this activity is also a target for potential antiviral agents. Thus, the teachings in the art suggest that an alternative solution to the problem of inhibiting HCV NS4B would be to inhibit GTPase activity of the protein if present.

The third finding is that those of ordinary skill in the art must have been able to pursue the known potential options with a reasonable expectation of success. In the present case, because the art teaches that many viral proteins, including other HCV viral proteins, with ATPase activity and similar nucleotide binding motifs also had GTPase activity, those in the art would have had a reasonable expectation of success in identifying the HCV NS4B protein as having GTPase activity in addition to the known ATPase activity, and that such activity could be targeted for the identification of potential inhibitors of NS4B activity. Moreover, in the present case, there are only two options as to the ability of NS4B to have GTPase activity. Either it does, or it does not. It would have been well within the skill of those of ordinary skill in the art to have made such a determination in the effort to identify inhibitors of this activity as potential inhibitor of HCV infection.

The Applicant further argues that, in making the rejection, no reason has been provided as to why those in the art would have attempted to identify inhibitors of GTPase activity as

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inhibitors of NS4B activity. This argument is not found persuasive. A rationale as to why those in the art would attempt to identify inhibitors of HCV NS4B activity by looking for inhibitors of GTPase activity was provided (i.e. the known association between ATPase and GTPase activities). Moreover, while the art indicates that not every protein with ATPase activity would also have GTPase activity, and while it could not be predicted to a point of surety if HCV NS4B had GTPase activity was present and “biologically relevant” as asserted by the Applicant, the teachings in the art provide adequate suggestion to render the claimed invention as obvious to try. This is because the art suggests that proteins having one activity may have the other activity, and also indicates that it may not always be clear which activity (ATPase or GTPase) a protein may have where an NTPase activity is suspected. Thus, it would have been obvious to those of ordinary skill in the art to have tried to identify inhibitors of HCV infection through the testing and identification of inhibitors of both NTPase activities.

The rejection is therefore maintained for the reasons above, and the reasons of record.

14. **(Prior Rejection- Maintained)** Claims 6 and 7 were rejected under 35 U.S.C. 103(a) as being unpatentable over Del Vecchio in view of Jin, Kadaré, and Rodriguez as applied to claims 1-4 above, and further in view of Morouianu et al. (PNAS 92:4318-22). Applicant traverses this rejection on substantially the same grounds as asserted with respect to claims 1 and 3 above. The arguments are not found persuasive for the same reasons described above. The rejection is therefore maintained.

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15. **(Prior Rejection- Maintained)** Claims 8-10 were rejected under 35 U.S.C. 103(a) as being unpatentable over Del Vecchio in view of Jin, Kadaré, and Rodriguez as applied to claims 1-4 above, and further in view of Wimmer et al. (U.S. 2002/0098202). This rejection is maintained over claims 8-10, and is extended to new claims 22 and 23.

Claim 22 reads on embodiments wherein the method comprises the use of a liver cell line. As Huh7 is a liver cell line, and as the art suggests the use of this cell line for making a determination as to whether a compound can inhibit HCV activity, claim 22 is rendered obvious for the same reasons as applied to claim 10 previously. Claim 23 reads on the method of claim 9, wherein the HCV is a live virus or a replicon. As the art as previously described renders obvious the use of HCV replicons for the identification of anti-HCV compounds, claim 23 is also obvious for the reasons described in the prior action.

Applicant traverses this rejection on substantially the same grounds as asserted with respect to claims 1 and 3 above, and provides further arguments as to why the claimed inventions would not have been obvious to try.

Applicant further traverses the rejection on the basis of the teachings of Kato, which indicated that the function of the NS4B protein was unknown. While this may be the case, the argument does not discredit the suggestion by Del Vecchio that the ATPase activity of NS4B may be targeted for the identification of potential anti-HCV therapeutics.

Further, with respect to the assertion that the ATPase activity appears to be a secondary activity of NS4B, the art indicates that where potential NTPase activity is found, it may often be unclear as to whether the target protein has ATPase, GTPase, or both activities. See, the references cited by the Applicant in support of the assertion that not all proteins with ATPase

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activity have GTPase activity, and the teachings of Moroianu et al. (PNAS 92:4318-22- indicating the reverse- reference cited in the prior action). Nonetheless, the teachings in the art indicate that the HCV NS4B protein has at an NTPase activity, and suggests targeting that activity for the identification of potential anti-HCV therapeutics. It would therefore have been obvious to those in the art to test both inhibitors of ATPase and GTPase activity to determine if such compounds inhibited HCV infections.

The arguments are not found persuasive for the reasons described above. The rejection is therefore maintained.

16. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

17. No claims are allowed. Claim 5 is objected to as depending from a rejected claim.

1. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

18. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is (571)272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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/Zachariah Lucas/
Primary Examiner, Art Unit 1648